PATENT

Attorney Docket No. 401865 (*formerly* 121-161)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Parikh et al.

Application No. 09/282,471

Art Unit: 1615

Examiner: Tran, Susan T.

Filed: November 8, 1999

For: FENOFIBRATE MICROPARTICLES

#19

DECLARATION UNDER 37 C.F.R. § 1.132
OF DR. ROBERT A. SNOW

Commissioner for Patents
Washington, D.C. 20231

I, Robert A. Snow, Ph.D., hereby state:

1. I am the Chief Scientific Officer of SkyePharma Canada Inc., a subsidiary of SkyePharma plc, which also owns the assignee of the subject application. I have been actively involved in professional chemistry-related (particularly pharmaceutical-related) research for over 25 years. I hold a Ph.D. in physical organic chemistry from York University (Toronto, Canada) and fulfilled a postdoctoral chemical research program at Ohio State University. A significant component of my professional and scientific activities have involved the development of microparticle and nanoparticle formulations for pharmaceutical and industrial applications.

2. I am familiar with the above-referenced patent application and its prosecution. I also have reviewed the amended claims submitted with this Declaration and have been advised of the substance of the Examiner Interview conducted on October 9, 2002. Specifically, I understand that during the interview the Examiners questioned whether mannitol must be present when producing fenofibrate microparticles according to the presently claimed method.

3. To address this question of whether mannitol is required to produce fenofibrate microparticles by the presently claimed method, the following experiment was performed under my direction in accordance with the guidance of the patent application, and specifically by applying the methods described in Examples 1-5, except as otherwise noted. A mixture of 10% w/w fenofibrate, 2% w/w Phospholipon 100H (pure hydrogenated soy phosphatidylcholine), and 2% w/w Tween 80 (polyoxyethylene sorbitan monooleate) (DI water was used to make the formulation qs to 100%) was subjected to particle size reduction using an Avestin Model C5 high pressure homogenizer, without the presence of any mannitol. After 2 hours processing, the smaller volume weighted mean particle size of the resultant microparticles was determined to be 1.04 μm +/- 0.1 μm.

4. For purposes of comparison, a similar experiment was performed by subjecting a mixture of 10% w/w fenofibrate and 2% w/w Phospholipon 100H (i.e., without mannitol and without Tween 80) to high pressure homogenization. After 2 hours processing, the volume weighted mean particle size of the resultant fenofibrate particles was 22.11 μm. In addition, the fenofibrate particles produced without Tween 80 were subject to significant agglomeration, which did not occur in the fenofibrate microparticles produced according to the method described in the subject patent application.

5. The results of the above-described experiments, considered in view of Example 1 in the subject application, indicate that by applying the presently claimed method as described in the subject patent application fenofibrate microparticles are obtained whether mannitol is present or not when such microparticles are produced. Moreover, the above-described experiments, particularly when considered in view of the experiments described in the subject application, demonstrate that applying a size-reducing energy to a mixture comprising fenofibrate particles, a phospholipid, and a nonphospholipid surfactant, produces fenofibrate microparticles having significantly smaller volume weighted mean particle size values than the volume weighted mean particle size values of fenofibrate particles produced by application of the same energy in the

presence of only a phospholipid without a nonphospholipid surfactant (as described above; see also Example A of the subject application).

6. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: November 4, 2002

Robert A. Snow, Ph.D.